c.) Remarks

The claims have been amended to recite the present invention with the specificity required by statute. No new matter has been added.

In the parent application, the specification was objected to for the use of the term "and the like". While the phrase is plainly accepted by the Patent and Trademark Office and well-known in all relevant arts,[1/] the specification has been amended to address the Examiner's concerns.

The Examiner previously rejected claims 16 and 17 under 35 USC §112, second paragraph, for utilizing the term "recombinant". The basis for this is unclear, such language is found throughout, e.g., the MPEP.

Additionally, the specification discloses *Escherichia coli* and *Saccharomyces cerevisiae* which express a glycosyltransferase gene derived from other organism, and COS7 cell line at page 14, line 2 up to page 15, line 8, and a recombinant line, such as namalwa cell line KJM-1 which contains a β1,3-galactosyltransaferase gene derived from human melanoma cell line WM266-4 at page 14 at lines 20-24. It would be apparent from technical usage and common knowledge that microorganisms which express a gene derived from other organism are "recombinant" *E. coli*, recombinant COS7 and the like. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 4 and 7 are rejected for the use of the phrase "either claims 2 and 3". Despite that such language is explicitly permitted by MPEP §608.01(n), that terminology has been deleted, solely in order to reduce the issues.

Claim 3 is rejected for the use of the terms "uridine diphosphate compound", "yeast", and the recitation "complex carbohydrate etc...or a treated product

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1/ Witness over 1,700,000 patents containing that phrase issued just from 1976 to date.

thereof". The Examiner's bases for these objections are believed to be addressed in the above amendment.

Previous claim 20 was rejected for lack of a biologic deposit. The Examiner states that Example 2 of the Japanese Published Unexamined Patent Application No. 181759/94 does not provide the source of KJM-1 namalwa cells and the starting plasmids used for the construction of plasmid pAMoERSAW1.

Respectfully submitted, such is incorrect; pAMoERASW1 is routinely prepared using pAGE107, pMOL1, pAGE207, pASN6, pPrAS1 and pAMoERC3Sc. None of these plasmids is proprietary; pAGE107 is prepared according to *Cytotechnology*, 3, 133 (1990) by using pAGE103 [*Journal of Biochemistry*, 101, 1307 (1987)], pAGE28 [*Journal of Biochemistry*, 101, 1307 (1987)], pUS19 [*Gene*, 33, 103 (1985)] and pKCR [*Proc. Natl. Acad. Sci. USA*, 78, 1527 (1981)].

pMOL1 is prepared according to Example 3 of JP-A-63394/89 using pMolp-1 [*Virology*, 141, 30 (1985)] and pBR322.

pAGE207 is prepared according to Example 1 in JP-A-181759/94 using pAGE107 and p201 [*Nature*, 313, 812 (1985)].

pASN6 is disclosed at col. 30, lines 12-17 of U.S. Patent 5,218,092.

Furthermore, pAMoERC3Sc is prepared using pAGE207ScN (which is obtained by introducing linker DNA into pAGE207, see Example 1 of JP-A-181759/94), pAMoERC3 (which is disclosed in Example 1 of JP-A-181759/94 and pAGE107.

Moreover, Namalwa KJM-1 can easily be prepared without experimentation according to page 134 of *Cytotechnology*, 3, 133 (1990).[2/]

Accordingly, these biological materials are all publicly available.

2/ Copies of all these papers are believed to be of record. However, if the Examiner wishes to receive additional copies or additional copies of translations, she is respectfully requested to inform the undersigned.

With respect to previous claim 3, the Examiner asserted that the specification does not teach how to simultaneously synthesize uridine diphosphate sugar and a complex carbohydrate by growing together yeast and animal cells, or yeast and bacterial cells, in the same aqueous medium, under the same temperature and pH conditions. In response, new claim 22 relates to producing a complex carbohydrate by adding a uridine diphosphate sugar recovered from a first aqueous medium to a second aqueous medium.

The Examiner also asserted the specification does not enable producing uridine diphosphate sugar or complex carbohydrate using "treated products" of *Saccharomyces* or *Kluyveromyces* cells. As well-understood, "cell" is a small mass of protoplasm bounded externally by a semipermeable membrane, usually including one or more nuclei and various other organelles with their products, capable alone of performing the fundamental functions of life. As such, the cell provides matter surrounded by a membrane structure which is isolated from the outside. It is noted the language objected to is "treated products <u>of</u>" cells, not "treated products <u>obtained from</u>" cells. Therefore, respectfully submitted, the Examiner's position in which the "dried product of the cells" includes separated components constituting the cell is unreasonable.

Previously, the Examiner maintained that the disclosure does not teach production of lacto-N-tetraose and lacto-N-neotetraose. However, Example 5 (up to page 23, line 15) discloses preparing complex carbohydrate by removing galactose at the non-reducing end of lacto-N-neotetraose with β-galatosidase to obtain GlcNAcb1-3Galb1-4Glc, which is used as a substrate of β1,3-galactosyltransferase and β1,4-galactosyltransferase. The last half of Example 5 clearly discloses producing lacto-N-tetraose using β1,3-galactosyltransferase (described in Example 4) purified from namalwa line KJM-

1/pAMoERSAW1[3/] as an enzyme source with the substrates UDP-Gal (described in Example 2) and GlcNAcb1-3b1-4Glc.

Since Examples 4 and 5 teach producing a complex carbohydrate using a glycosyltransferase obtained from a recombinant cell having a glycosyltransferase gene, and the specification discloses (page 14, line 13 to page 15, line 8) examples of recombinant cells that express β1,4-galactosyltransferase, those of ordinary skill understood from the specification as filed that lacto-N-neotetraose can be prepared by the method described in Example 3 with such recombinant cells.[4/]

Previous claims 2, 7, and 8 were rejected as being obvious over Caputto or Herscovics in view of common knowledge in the art. The Examiner asserts that because Caputto shows that baker's yeast produces uridine diphosphate glucose, and it would have been obvious to cultivate baker's yeast with uridine diphosphate glucose precursors to produce a uridine diphosphate sugar. Similarly, because Herscovics teaches that *S. cerevisiae* can synthesize sugar donors, the Examiner contends it would have been obvious to cultivate *S. cerevisiae* in a medium with uridine diphosphate glucose precursors to produce a uridine diphosphate sugar.

Finally, claims 3, 4, 7, 8, 11, and 16 were rejected as being obvious over Tochikura in view of the common knowledge in the art, and further in view of Ichikawa. The Examiner asserts that because Tochikura teaches *S. cerevisiae* fermentation as an efficient way of producing UDP glucose, and UDP sugars are important in carbohydrates synthesis, and because Ichikawa discloses *E. coli* cells that express ceramide β1-1' glucosyltransferase, it would have been obvious to utilize *S. cerevisiae* culture as the

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3/ Many β1,3-galactosyltransferases were known at the time the present application was made as shown in the search results of *Ovid: Bibliographic Records* attached at Tab A.

4/ If it will be helpful to the Examiner, Applicants will be happy to provide a Declaration under Rule 132 by one of ordinary skill, in order to evidence the same and complete the record.

source of UDP glucose with *E. coli* transformed with human ceramide β1-1' glucosyltransferase.

These rejections are each respectfully traversed, as discussed below.

First, Caputto only discloses that UDP-glucose is present in yeast cells cultured in the ordinary medium and that UDP-glucose in the cells can be extracted by toluene. However, new claim 21 recites conducting an enzyme reaction using a yeast cell, a nucleotide precursor and a sugar to form and accumulate UDP-glucose in an aqueous medium outside of the yeast cell. Accordingly, Caputto does not suggest that the yeast cell incorporates the substrate nucleotide precursor from outside the cell and produce UDP-glucose extracellularly using glucose as another substrate.

Herscovics proffer that *Saccharomyces cerevisiae* biosynthesizes UDP-GlcNAc intracellularly from the sugar chain structure of *S. cerevisiae.* However, Herscovics does not suggest that yeast incorporates a nucleotide precursor from outside of the cell and has activity of extracellularly producing UDP-GlcNAc using maltose and glucosamine as substrates.

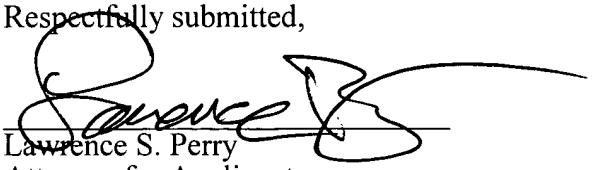
Tochikura shows that ground yeast cells synthesize UDP-sugar from UMP. However, Tochikura does not suggest that orotic acid, orotidine, uridine and uracil (including UMP) are incorporated into a yeast cell through cell membrane.

Claims 21, 22 and 24-33 remain presented for continued prosecution.

Entry hereof is earnestly solicited.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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